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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/750,092	12/31/2003	Zhandong Don Zhong	034827-0112	1890

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FOLEY & LARDNER LLP
P.O. BOX 80278
SAN DIEGO, CA 92138-0278

EXAMINER

BAUGHMAN, MOLLY E

ART UNIT	PAPER NUMBER
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1637

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/30/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/750,092

Applicant(s)

ZHONG ET AL.

Examiner

Molly E. Baughman

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 January 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 28-30 and 40-68 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 28-30 and 40-68 is/are rejected.
- 7) ☐ Claim(s) 50-52, 66 and 67 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>1/17/2007</u> . | 6) <input type="checkbox"/> Other: _____ |

1. Applicant's arguments and amendments, filed 1/17/2007, with respect to the rejection(s) of claim(s) 28-32 under 35 USC 102(b) and 35 USC 103 have been fully considered and are withdrawn in view of the amendments. However, a new ground(s) of rejection is made in view of the amendments.
2. Applicant's addition of new claims 40-68, and cancellation of claims 1-27 and 31-39 in the reply filed on 1/17/2007 is acknowledged.
3. Currently, claims 28-30 and 40-68 are under examination.

Specification

4. The disclosure is objected to because of the following informalities: the word "sucinimidyl" is spelled incorrectly numerous times, and should read "succinimidyl." Specific examples are found on pgs. 12, [0027], pg. 13, [0031], and claims 50-51 and 66-67 (see below). Appropriate correction is required.

Claim Objections

5. Claim 52 is objected to because of the following informality: the claim depends from claim 38, which has been cancelled. Accordingly, claim 52 has not been further treated on the merits.
6. Claims 50-51, and 66-67 are objected to because of the following informalities: the word "sucinimidyl" is spelled incorrectly, and should read "succinimidyl." Correction is required.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 28-30, 40-43, 45-46, 53-59, 61-65, and 68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eberie et al (US 5,413,906) in view of Bodepudi et al. (US 2004/0171040 A1).

Eberie et al. teach a kit containing a template nucleic acid (which can be DNA or RNA, as well as homopolymeric or heteropolymeric – col.3, lines 8-21), at least one detectable and one immobilizable mononucleoside triphosphate, and preferably a primer, wherein neither the RNA template nor the DNA primer contains a detectable or luminescent moiety (column 8, lines 23-65). The kit also contains reagents for

Art Unit: 1637

detection, such as pH-buffer, detergent, complex former, co-factors, salts, anti-oxidizing agents, and streptavidin coated cuvette, tube, pellets, or microtiter plate (column 8, lines 37-60). Specific examples describe an RT-buffer comprising 5mM of $MgCl_2$ (Column 14, lines 47-49). The mononucleoside triphosphates are triphosphates of nucleosides, which can contain natural bases such as adenine, guanine, cytosine, and uracil or thymine (column 3, lines 34-49), which can be detectable through a dye, a fluorescent label or a component of an immunologic reaction such as an antigen, antibody or hapten, or a covalently bound non-radioactive chemical group. The immobilizable mononucleoside triphosphates can be covalently bound chemical groups which have a specific affinity for a solid phase, i.e. immobilizable through binding partners such as biotin-avidin, biotin-streptavidin, antigen-antibody, hapten-antibody, etc (column 4, lines 1-20).

Eberie does not describe a kit wherein the detectable deoxynucleoside triphosphate is labeled with an acridinium moiety (claims 1, 46-49, 53, and 62-65),

Bodepudi et al. teach labeling a deoxynucleoside triphosphate with an acridinium moiety. They also teach the deoxynucleoside triphosphate labeled with an acridinium moiety having the formula TP-Sugar-Px-L-Acr wherein: TP is a triphosphate group attached to the 5' position of the sugar; sugar is a pentose sugar moiety; Px is a purine, pyrimidine, or 7-deazapurine, and wherein Px is attached to the 1' position of the sugar moiety through the N1 position of Px when Px is a pyrimidine or through the N9 position of Px when Px is a purine or a 7-deazapurine; L is a linker comprising linear or branched hydrocarbylene or heterocarbylene of at least one carbon atom, wherein L is

covalently attached to Acr at one end of L, and at another end to Px through position C5 or C6 of Px when Px is a pyrimidine, or through position C8 of Px when Px is a purine, or through position C7 or C8 of Px when Px is a 7-deazapurine; and Acr is an acridinium moiety (pg.1 [0007], pg. 2 [0026-0036], pg.5 [0094] and [0098], pg.7 [0016] and [0118]).

One of ordinary skill in the art would have been motivated to modify the kit of Eberie et al. to include a deoxynucleotide triphosphate labeled with an acridinium moiety and having the formula of TP-Sugar-Px-L-Acr because Bodepudi et al. demonstrate that labeling a deoxynucleoside triphosphate with an acridinium moiety for chemiluminescence detection was well known in the art, and specifically further teach a deoxynucleotide triphosphate labeled with an acridinium moiety having the formula TP-Sugar-Px-L-Acr and including it within a kit (pg. 34 [0368-0369]). The skilled artisan would have had a reasonable expectation of success in modifying the kit of Eberie et al. to use a deoxynucleoside triphosphate with an acridinium moiety having the formula TP-Sugar-Px-L-Acr in the kit of Eberie et al. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the make a kit and include the claimed a deoxynucleotide triphosphate labeled with an acridinium moiety having the formula TP-Sugar-Px-L-Acr therein.

10. Claims 47-49, and 63-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eberie et al (US 5,413,906) in view of Bodepudi et al. (US 2004/0171040 A1) as applied to claims 28-30, 40-43, 45-49, 53-59, 61-65, and 68 above, and further in view of Petrie et al. (US 5,824,796).

The teachings of the primary references are discussed above. Although Bodepudi et al. describe linkers including hydrocarbons (pg.28, [0308]), they do not teach a linker that is a linear hydrocarbylene or heterocarbylene comprising one carbon atom (claim 47 and 63), or a linker that is a linear alkenylene or heteroalkenylene comprising at least 3 carbon atoms (claim 48 and 64), or wherein the linker is selected from the group consisting of $-\text{CH}_2\text{-CH=CH-CH}_2-$, $-\text{CH=CH-CH}_2\text{-NH-}$, $-\text{NH}(\text{CH}_2)_6\text{NH-}$, $-\text{C}\equiv\text{C-CH}_2\text{NH-}$, and $-\text{CH}_2\text{-C}\equiv\text{C-CH}_2-$ (claim 49 and 65).

Petrie teaches using various linkers to attach a nucleobase to a label, wherein such a label is an acridinium ester (column 9, lines 29-55; column 11, lines 15-20; column 13, lines 64-67; and column 14, lines 49-50). Such linkers include a linear alkenylene or heteroalkenylene comprising at least 3 carbon atoms, or wherein the linker is selected from the group consisting of $-\text{CH}_2\text{-CH=CH-CH}_2-$, $-\text{CH=CH-CH}_2\text{-NH-}$, $-\text{NH}(\text{CH}_2)_6\text{NH-}$, $-\text{C}\equiv\text{C-CH}_2\text{NH-}$, and $-\text{CH}_2\text{-C}\equiv\text{C-CH}_2-$ (column 10, lines 27-43).

One of ordinary skill in the art would have been motivated to modify the kit of Eberie et al. and Bodepudi et al. to include a deoxynucleotide triphosphate labeled with an acridinium moiety having the formula TP-Sugar-Px-L-Acr which has a linker that is a linear hydrocarbylene or heterocarbylene comprising one carbon atom, or a linker that is a linear alkenylene or heteroalkenylene comprising at least 3 carbon atoms or wherein the linker is selected from the group consisting of $-\text{CH}_2\text{-CH=CH-CH}_2-$, $-\text{CH=CH-CH}_2\text{-NH-}$, $-\text{NH}(\text{CH}_2)_6\text{NH-}$, $-\text{C}\equiv\text{C-CH}_2\text{NH-}$, and $-\text{CH}_2\text{-C}\equiv\text{C-CH}_2-$ because Petrie et al. demonstrate that it was well known in the art to use linkers including alkenylene groups for attaching labels such as acridinium esters to nucleobases. The skilled artisan would

Art Unit: 1637

have had a reasonable expectation of success in using a linker in the deoxynucleotide triphosphate labeled with an acridinium moiety having the formula TP-Sugar-Px-L-Acr that is a linear hydrocarbylene or heterocarbylene comprising one carbon atom, or a linker that is a linear alkenylene or heteroalkenylene comprising at least 3 carbon atoms or wherein the linker is selected from the group consisting of $-\text{CH}_2-\text{CH}=\text{CH}-\text{CH}_2-$, $-\text{CH}=\text{CH}-\text{CH}_2-\text{NH}-$, $-\text{NH}(\text{CH}_2)_6\text{NH}-$, $-\text{C}\equiv\text{C}-\text{CH}_2\text{NH}-$, and $-\text{CH}_2-\text{C}\equiv\text{C}-\text{CH}_2-$ in the kit of Eberie et al. and Bodepudi et al. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to make a kit and use the claimed hydrocarbylene linker in the deoxynucleotide triphosphate labeled with an acridinium moiety having the formula TP-Sugar-Px-L-Acr therein.

11. Claims 44, 50-51, 60, and 66-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eberie et al (US 5,413,906) in view of Bodepudi et al. (US 2004/0171040 A1) as applied to claims 28-30, 40-43, 45-49, 53-59, 61-65, and 68 above, and further in view of Nelson et al., "Simultaneous Detection of Multiple Nucleic Acid Targets in a Homogeneous Format," Biochemistry, 1996, Vol.35, pp.8429-8438.

The teachings of the primary references are discussed above. Although Bodepudi et al. describe an acridinium ester as a label, they do not teach the acridinium moiety selected from the group consisting of 4-(2-succinimidyl-oxycarbonyl)ethyl-phenyl- 10-acridinium-9-carboxylate trifluoromethyl sulfonate, 1-methyl-acridinium ester, and 1-methyl-di-meta-fluoro-acridinium ester (claims 50-51, and 66-67). They also do not describe the kit further comprising a dilute acid, hydrogen peroxide, or both (claims 44 and 60).

Nelson et al. teach probes comprising nucleotide bases labeled with various acridinium esters. Such acridinium esters include 4-(2-succinimidyl-oxycarbonyl-ethyl)-phenyl- 10-methylacridinium-9-carboxylate trifluoromethyl sulfonate, 1-methyl-acridinium ester, and 1-methyl-di-meta-fluoro-acridinium ester (pg.8431-8432, "Preparation of 4-(2-succinimidyl-oxycarbonyl-ethyl)-phenyl- 10-methylacridinium-9-carboxylate trifluoromethyl sulfonate" and "Simultaneous Detection of Two Acridinium Ester-Labeled DNA Probes"). Nelson et al. also teach detecting the acridinium ester labeled nucleotides by chemiluminescence via the addition of 200ul of 0.4N HCl and 0.1% H₂O₂ (pg. 8432, "Characterization of the Differential Hydrolysis Properties of Acridinium Ester-Labeled DNA Probes"), or detection reagent 1 - 200ul of 0.1% H₂O₂, 1mM HNO₃ (pg.8431, "Characterization of the Chemiluminescence Properties of Various Acridinium Ester-Labeled DNA Probes").

One of ordinary skill in the art would have been motivated to modify the kit of Eberie et al. and Bodepudi et al. to include a deoxynucleotide triphosphate labeled with an acridinium moiety having the formula TP-Sugar-Px-L-Acr, wherein the acridinium moiety is 4-(2-succinimidyl-oxycarbonyl-ethyl)-phenyl- 10-acridinium-9-carboxylate trifluoromethyl sulfonate, 1-methyl-acridinium ester, or 1-methyl-di-meta-fluoro-acridinium ester, as well as a dilute acid, and hydrogen peroxide because Nelson et al. demonstrate that such acridinium ester labels and detection of such acridinium ester labels via dilute acids and hydrogen peroxide was well known in the art. The skilled artisan would have had a reasonable expectation of success in using 4-(2-succinimidyl-oxycarbonyl-ethyl)-phenyl- 10-acridinium-9-carboxylate trifluoromethyl sulfonate, 1-

Art Unit: 1637

methyl-acridinium ester, or 1-methyl-di-meta-fluoro-acridinium ester as a label of the deoxynucleotide triphosphate labeled with an acridinium moiety having the formula TP-Sugar-Px-L-Acr within the kit of Eberie et al. and Bodepudi et al. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to make a kit and use the claimed 4-(2-succinimidyl-oxycarbonylethyl)-phenyl- 10-acridinium-9-carboxylate trifluoromethyl sulfonate, 1-methyl-acridinium ester, or 1-methyl-di-meta-fluoro-acridinium ester as the acridinium moiety therein.

Summary

12. No claims are free of the prior art.

Conclusions

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

Art Unit: 1637

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Molly E. Baughman whose telephone number is 571-272-4434. The examiner can normally be reached on Monday-Friday 8-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Molly E Baughman
Examiner
Art Unit 1637

MEB 3/22/07

Kenneth R. Horlick
KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

3/26/07